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Note

Synthesis of novel isoxazolyl 1,3,5-benzoxadiazocine-4-thiones as possible biodynamic agents

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Synthesis of novel isoxazolyl 1,3,5-benzoxadiazocine-4-thiones **5** has been accomplished by condensation of 4-amino-3-methyl-5-styrylisoxazole **1** with salicylaldehydes, followed by reduction, treatment with arylisothiocyanates and subsequent ring closure in the presence of formaldehyde. The methodology used in this synthesis is the first approach of its kind towards the synthesis of title compounds.

Keywords: isoxazolyl 1,3,5-benzoxadiazocine-4-thiones, Schiff bases, reduction, amino thiophenols, ring closure.

The chemistry of heterocycles lies at the heart of drug discovery[1]. Many known active compounds contain heterocyclic cores, which are indispensable elements for bioactivity[2]. Benzoxadiazocines have been claimed to exhibit sedative, muscle relaxant and anticonvulsant effects[3]. Oxadiazocines are shown to act as bacteriocides, hypnotic agents[4], central nervous system stimulants[5] and are also known to possess pharmacological activity[6]. The biological importance and considerable therapeutic potential of these compounds generated interest in designing the synthesis of a number of derivatives[7], which might become potential drug candidates as inhibitors of HIV-1 reverse transcriptase[8]. Very recently, oxadiazocines are reported to have been utilized as immuno therapeutics, antimicrobial drugs and vaccines[9].

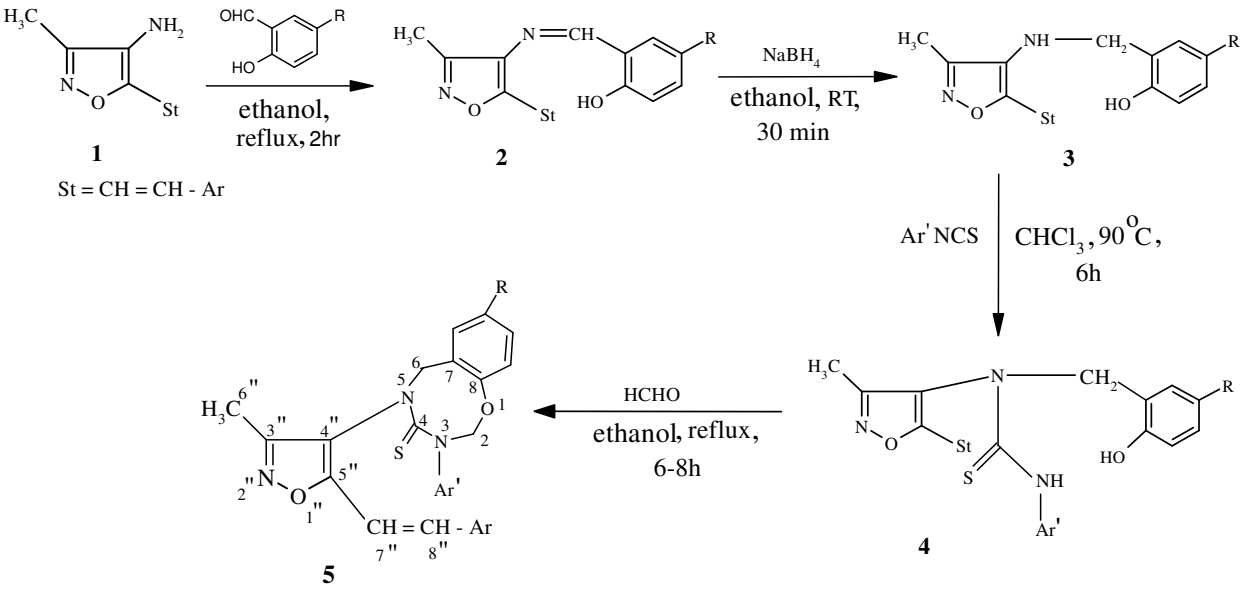
Similarly, isoxazole nucleus can be found frequently in the structure of numerous naturally occurring and synthetic compounds with interesting biological and pharmacological properties[10]. Additionally, isoxazole moiety displays a wide range of organic reactivities and could be used as a effective means of preparing new molecular scaffolds[11]. Isoxazoles have been repeatedly shown as useful synthons in organic synthesis[12]. In spite of such a high potential significance for benzoxadiazocines and oxadiazocines, a survey of literature showed that little attention has been given towards the synthesis of this class of heterocyclic compounds. In view of this, and as a sequel to our work on the synthesis of a variety of heterocycles linked to isoxazole moiety[13], we undertook the synthesis of isoxazolyl benzoxadiazocines in order to explore the pharmacological activity of these compounds. Herein, the results on the synthesis of isoxazolyl 1,3,5-benzoxadiazocines is reported by adopting simple methodology.

Results and Discussion

The reaction of 4-amino-3-methyl-5-styrylisoxazole **1** with substituted salicylaldehydes in refluxing alcohol led to the formation of Schiff bases *viz.,* 2-[(3-methyl-5-[*E*]-2-aryl-1-ethenyl]-4-isoxazolylimino)-methyl] phenols **2** in quantitative yields. The Schiff bases **2** on treatment with sodium borohydride underwent reduction of imine to amine, resulting in the formation of 2-[(3-methyl-5-[*E*]-2-aryl-1-ethenyl]-4-isoxazolylamino)-methyl] phenols **3** in moderate to good yields. The nucleophilic addition of amino methyl phenols **3** with aryl isothiocyanates in hot chloroform led to the formation of *N*-(2-hydroxy-benzyl)–*N*-3–methyl-5-[(*E*)-2-aryl-1-ethenyl]-4–iso-xazolyl–*N*′-aryl thioureas **4**. The thioureas **4** on heating with formaldehyde in methanol solution underwent smooth ring closure, involving internal Mannich reaction, to give novel 5(3-methyl-5-[(*E*)-2-aryl-1-ethenyl]4-isoxazolyl-3-aryl-3,4,5,6-tetrahydro-2*H*-1,3,5-benzoxadiazocine-4-thiones **5** in moderate to good yields (**Scheme I**).

The structural assignments of the new compounds were based on their elemental analysis **(Tables I** and **II)** and spectral data **(Tables III** and **IV)**.

The formation of Schiff's base **2** from 4-amino-3-methyl-5-styrylisoxazole **1** was confirmed from its IR, ^{1}H NMR, mass spectral data and elemental analysis. IR spectrum of **2** showed absorption bands at 1617 and 3400 cm^{-1} due to C=N and OH respectively, while its ^{1}H NMR spectrum exhibited a sharp singlet at 9.05 and a broad singlet at δ 12.25 which correspond to azomethine and hydroxyl protons respectively. Mass spectrum of **2** showed molecular ion peak $[M+H]^+$ at *m*/*z* 305. Further, conversion of **2** to amino methyl



1 **2** **3** **4** **5**

2, 3a = R = H, Ar = C_6H_5
2, 3b = R = CH_3, Ar = C_6H_5
2, 3c = R = OCH_3, Ar = C_6H_5
2, 3d = R = H, Ar =4-Cl C_6H_5,
2, 3e = R = H, Ar = 4-CH_3 C_6H_4,
2, 3f= R = H, Ar = 4- $CH_3OC_6H_4$

4, 5a = R = H, Ar = C_6H_5, Ar' = C_6H_5
4, 5b = R = H, Ar = C_6H_5, Ar'= 4-Cl-C_6H_4
4, 5c = R = H, Ar = C_6H_5, Ar'= 4-Br-C_6H_4
4, 5d =R = H, Ar = C_6H_5, Ar'= 4-CH_3-C_6H_5
4, 5e = R = CH_3, Ar = C_6H_5, Ar'= C_6H_5
4, 5f = R = OCH_3, Ar = C_6H_5, Ar' = C_6H_5
4, 5g = R = CH_3, Ar = 4-ClC_6H_4, Ar' = C_6H_5
4, 5h = R = OCH_3, Ar = 4-$CH_3C_6H_4$, Ar' = C_6H_5

Scheme I

Table I — Physical data of compounds **2** and **3**

Product	R	Ar	m.p. (^{0}C)	Yield (%)	Mol.formula (Mol.wt.)	Found (Calcd) (%) C	H	N
2a	H	C_6H_5	60-62	85	$C_{19}H_{16}N_2O_2$	75.04 (75.00	5.30 5.26	9.26 9.21)
2b	CH_3	C_6H_5	72-74	85	$C_{20}H_{18}N_2O_2$	75.41 (75.47	5.60 5.66	8.77 8.80)
2c	OCH_3	C_6H_5	81-83	85	$C_{20}H_{18}N_2O_3$	71.80 (71.85	5.34 5.38	8.40 8.38)
2d	H	4-ClC_6H_4	88-90	80	$C_{19}H_{15}N_2O_2Cl$	67.41 (67.45	4.47 4.43	8.84 8.38)
2e	H	4- $CH_3C_6H_4$	95-97	80	$C_{20}H_{18}N_2O_2$	75.41 (75.47	5.62 5.66	8.84 8.80)
2f	H	4- $OCH_3C_6H_4$	85-87	75	$C_{20}H_{18}N_2O_3$	71.82 (71.85	5.34 5.38	8.32 8.38)
3a	H	C_6H_5	68-70	80	$C_{19}H_{18}N_2O_2$	74.48 (74.50	5.84 5.88	9.12 9.15)
3b	CH_3	C_6H_5	58-60	80	$C_{20}H_{20}N_2O_2$	75.06 (75.00	6.21 6.25	8.79 8.75)
3c	OCH_3	C_6H_5	83-85	80	$C_{20}H_{20}N_2O_3$	71.46 (71.42	5.91 5.95	8.24 8.29)
3d	H	4-ClC_6H_4	97-99	80	$C_{19}H_{17}N_2O_2Cl$	67.00 (67.05	5.04 5.00	8.29 8.23)
3e	H	4-$CH_3C_6H_4$	64-66	80	$C_{20}H_{20}N_2O_2$	75.03 (75.00	6.28 6.25	8.71 8.75)
3f	H	4- $OCH_3C_6H_4$	82-84	85	$C_{20}H_{20}N_2O_3$	71.44 (71.42	5.90 5.95	8.38 8.29)

Table II — Physical data of compounds **4** and **5**

Product	R	Ar	Ar'	m.p. (°C)	Yield (%)	Mol.formula (Mol.wt.)	Found (Calcd) (%) C	H	N
4a	H	C_6H_5	C_6H_5	100-02	85	$C_{26}H_{23}N_3O_2S$	70.69 (70.74	5.26 5.21	9.48 9.52)
4b	H	C_6H_5	4-ClC_6H_4	116-18	85	$C_{26}H_{22}N_3O_2SCl$	65.62 (65.68	4.64 4.63	8.86 8.84)
4c	H	C_6H_5	4-BrC_6H_4	133-35	80	$C_{26}H_{22}N_3O_2SBr$	60.08 (60.11	4.26 4.23	8.05 8.09)
4d	H	C_6H_5	4-$CH_3C_6H_4$	120-22	80	$C_{27}H_{25}N_3O_2S$	71.26 (71.20	5.44 5.49	9.20 9.23)
4e	CH_3	C_6H_5	C_6H_5	137-39	80	$C_{27}H_{25}N_3O_2S$	71.24 (71.20	5.42 5.49	9.22 9.23)
4f	OCH_3	C_6H_5	C_6H_5	127-29	80	$C_{27}H_{25}N_3O_3S$	68.74 (68.78	5.33 5.30	8.94 8.91)
4g	CH_3	4- ClC_6H_4	C_6H_5	122-25	85	$C_{27}H_{24}N_3O_2SCl$	66.21 (66.25	4.94 4.90	8.62 8.58)
4h	OCH_3	4-$CH_3C_6H_4$	C_6H_5	128-30	80	$C_{28}H_{27}N_3O_3S$	69.30 (69.27	5.59 5.56	8.70 8.65)
5a	H	C_6H_5	C_6H_5	138-40	85	$C_{27}H_{23}N_3O_2S$	71.58 (71.52	5.01 5.07	9.23 9.27)
5b	H	C_6H_5	4-ClC_6H_4	145-47	80	$C_{27}H_{22}N_3O_2SCl$	66.48 (66.52	4.51 4.54	8.57 8.62)
5c	H	C_6H_5	4- BrC_6H_4	160-62	80	$C_{27}H_{22}N_3O_2SBr$	61.04 (61.01	4.17 4.14	7.93 7.90)
5d	H	C_6H_5	4- $CH_3C_6H_4$	141-43	85	$C_{28}H_{25}N_3O_2S$	71.90 (71.94	5.37 5.35	8.97 8.99)
5e	CH_3	C_6H_5	C_6H_5	155-57	80	$C_{28}H_{25}N_3O_2S$	71.96 (71.94	5.31 5.35	8.94 8.99)
5f	OCH_3	C_6H_5	C_6H_5	165-67	80	$C_{28}H_{25}N_3O_3S$	69.51 (69.56	5.12 5.17	8.74 8.69)
5g	CH_3	4-ClC_6H_4	C_6H_5	143-45	85	$C_{28}H_{24}N_3O_2SCl$	67.08 (67.06	4.74 4.79	8.42 8.38)
5h	OCH_3	4- $CH_3C_6H_4$	C_6H_5	162-63	80	$C_{29}H_{27}N_3O_3S$	70.06 (70.02	5.49 5.43	8.40 8.45)

phenols **3** was confirmed from its IR spectrum which showed peaks at 3450 and 3260 cm^{-1} indicating the presence of NH and OH functional groups respectively. In its ^1H NMR spectrum, peaks due to NH and CH_2 protons appeared at δ 3.20 and 4.24 respectively. Compound **3** displayed molecular ion peak $[M+H]^+$ at *m/z* 307.

Further, the formation of **4** from **3** was confirmed by its IR spectrum which showed absorption bands at 1225, 3240 and 3180 cm^{-1} due to C=S, NH and OH groups respectively. In its ^1H NMR spectrum **4**, peaks due to NH and OH protons appeared at δ 8.98 and 9.80 respectively as broad singlets. The mass spectrum of **4** exhibited the molecular ion peak $[M+H]^+$ at *m/z* 442. Cyclization of **4** to title compounds *viz.,* 1,3,5-benzoxadiazocine-4-thiones **5** was confirmed from its IR and ^1H NMR spectrum which did not show absorption bands due to NH and OH and did not exhibit the signals at δ 8.98 and 9.80, which are present in its precursor respectively. Further, the mass spectrum of **5** fully agrees with the cyclic structure by showing the molecular ion $[M^+]$ peak at *m/z* 453. ^{13}C NMR spectrum of **5** confirms the formation of 1,3,5-benzoxadiazocine **(Table IV)**.

Conclusion

It can be concluded that a simple and efficient method is adopted to synthesize isoxazolyl 1,3,5-benzoxadiazocines in good yields under mild conditions. These compounds may be applied as drugs and the activity data will be published elsewhere. This happens to be the first report and the

Table III — IR, ^{1}H NMR and MS spectral data for compounds **2** and **3**

Compds	IR(KBr cm^{-1})	^{1}H NMR (δ) (300 MHz $CDCl_3$)	MS $[M+H]^+$
2a	1607(C=N) 3400 (OH)	2.38 (s, 3H, CH_3), 6.98 (d, *J* = 12 Hz, 1H, CH=CH), 7.15 (d, *J* = 12 Hz, 1H, CH =CH), 7.40-7.82 (m, 9H, Ar-H), 9.05 (s, 1H, N = CH), 12.25 (bs, 1H, OH, D_2O exchangeable).	305
2a	1620(C=N) 3335 (OH)	2.28 (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 6.85 (d, *J* = 12 Hz, 1H, CH = CH), 7.02 (d, *J* = 12 Hz, 1H, CH=CH), 7.35-7.67 (m, 8H, Ar-H), 9.00 (s, 1H, N=CH), 12.20 (bs, 1H, OH, D_2O exchangeable).	319
2c	1615(C=N) 3380 (OH)	2.38 (s, 3H, CH_3), 3.80 (s, 3H, OCH_3), 6.80 (d, *J* = 12 Hz, 1H, CH=CH), 7.21 (d, *J* = 12 Hz, 1H, CH=CH), 7.25-7.80 (m, 8H, Ar-H), 8.95 (s, 1H, N = CH), 12.05 (bs, 1H, OH, D_2O exchangeable).	335
2d	1618(C=N) 3385 (OH)	2.40 (s, 3H, CH_3), 6.82 (d, *J* = 12 Hz, 1H, CH=CH), 6.95 (d, *J* = 12 Hz, 1H, CH=CH), 7.20-7.65 (m, 8H, Ar-H), 9.02 (s, 1H, N=CH), 12.00 (bs, 1H, OH, D_2O exchangeable).	339
2e	1620(C=N) 3390 (OH)	2.30 (s, 3H, CH_3), 2.48 (s, 3H, CH_3), 6.68 (d, *J* = 12 Hz, 1H, CH=CH), 6.82 (d, *J* = 12 Hz, 1H, CH=CH), 7.05-7.55 (m, 8H, Ar-H), 8.95 (s, 1H, N = CH), 12.05 (bs, 1H, OH, D_2O exchangeable).	319
3a	3450 (NH) 3260 (OH)	2.25 (s, 3H, CH_3), 3.20 (bs, 1H, NH, D_2O exchangeable), 4.24 (s, 2H, CH_2), 6.90 (d, *J* = 12 Hz, 1H, CH=CH), 7.10 (d, *J* = 12 Hz, 1H, CH=CH), 7.20-7.58 (m, 9H, Ar-H), 8.85 (bs, 1H, OH, D_2O exchangeable).	307
3b	3410 (NH) 3280 (OH)	2.30 (s, 3H, CH_3), 2.45(s, 3H,CH_3), 3.45 (bs, 1H, NH, D_2O exchangeable), 4.25 (s, 2H, CH_2), 6.85 (d, *J* = 12 Hz, 1H, CH=CH), 6.90 (d, *J* = 12 Hz, 1H, CH=CH), 7.02-7.62 (m, 8H, Ar-H), 8.89 (bs, 1H, OH, D_2O exchangeable).	321
3c	3425 (NH) 3300 (OH)	2.32 (s, 3H, CH_3), 3.50 (bs, 1H, NH, D_2O exchangeable), 3.80 (s, 3H, OCH_3), 4.22 (s, 2H, CH_2), 6.70 (d, *J* = 12 Hz, 1H, CH=CH), 6.85 (d, *J* = 12 Hz, 1H, CH=CH), 7.00-7.55 (m, 8H, Ar-H), 9.05 (bs, 1H, OH, D_2O exchangeable).	337
3d	3430 (NH) 3315 (OH)	2.38 (s, 3H, CH_3), 3.45 (bs, 1H, NH, D_2O exchangeable), 4.30 (s, 2H, CH_2), 6.82 (d, *J* = 12 Hz, 1H, CH=CH), 6.95 (d, *J* = 12 Hz, 1H, CH=CH), 7.05-7.60 (m, 8H, Ar-H), 9.25 (bs, 1H, OH, D_2O exchangeable).	341
3e	3400 (NH) 3315 (OH)	2.36 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 3.58 (bs, 1H, NH, D_2O exchangeable), 4.25 (s, 2H, CH_2), 6.65 (d, *J* = 12 Hz, 1H, CH= H), 6.75 (d, *J* = 12 Hz, 1H, CH= CH), 6.90-7.45 (bs, 1H, OH, D_2O exchangeable).	321

Table IV— IR, ^{1}H NMR, MS and ^{13}C NMR spectral data for compounds **4** and **5**

Compds	IR(KBr cm^{-1})	^{1}H NMR (δ) (300 MHz $CDCl_3$)	MS $[M+H]^+$
4a	3225 (NH) 3180 (OH) 1190(C=S)	2.25 (s, 3H, CH_3), 5.20 (s, 2H, CH_2), 6.80 (d, 1H, *J* = 12Hz, CH=CH), 6.95 (d, 1H, *J* = 12 Hz, CH=CH), 7.00-7.65 (m, 15H, ArH), 8.60 (bs, 1H, NH, D_2O exchangeable), 9.50 (bs, 1H, OH, D_2O exchangeable).	442
4b	3215 (NH) 3120 (OH) 1110(C=S)	2.30 (s, 3H, CH_3), 5.32 (s, 2H, CH_2), 6.70 (d, 1H, *J* = 12Hz, CH=CH), 6.82 (d, 1H, *J* = 12Hz, CH = CH), 7.20-8.11(m, 14H, ArH), 8.20 (bs, 1H, NH, D_2O exchangeable), 9.41 (bs, 1H, OH, D_2O exchangeable).	476
4c	3220 (NH) 3210 (OH) 1125(C=S)	2.25 (s, 3H, CH_3), 5.51 (s, 2H, CH_2), 6.68 (d, 1H, *J* = 12Hz, CH=CH), 6.80 (d, 1H, *J*=12Hz, CH = CH), 7.00-7.12 (m, 14H, ArH), 8.90 (bs, 1H, NH, D_2O exchangeable), 9.65(bs, 1H, OH, D_2O exchangeable.	520
4d	3275 (NH) 3235 (OH) 1150(C=S)	2.31 (s, 3H, CH_3), 2.45 (s, 3H, CH_3) 5.02 (s, 2H, CH_2), 6.72 (d, 1H, *J* = 12Hz, CH=CH), 6.88 (d, 1H, *J* = 12Hz, CH = CH), 7.20-7.83(m, 14H, ArH), 8.92 (bs, 1H, NH, D_2O exchangeable), 9.52 (bs, 1H, OH, D_2O exchangeable).	456
4e	3220 (NH) 3230 (OH) 1130(C=S)	2.32 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 5.50 (s, 2H, CH_2), 6.68 (d, 1H, *J* = 12Hz, CH=CH), 6.79 (d, 1H, *J* = 12Hz, CH=CH), 7.17-8.26 (m, 14H, ArH), 8.50 (bs, 1H, NH, D_2O exchangeable), 9.21(bs, 1H, OH, D_2O exchangeable).	456
5a	1200(C=S) 1120 (C-O)	2.28 (s, 3H, CH_3), 4.50 (s, 2H, NCH_2), 6.00 (s, 2H, OCH_2), 6.80 (d, 1H, *J* = 12Hz, CH=CH), 6.92 (d, 1H, *J* = 12 Hz, CH=CH), 7.10-7.60 (m, 15H, ArH).	453[M^+]

—Contd

Table IV— IR, ^{1}H NMR, MS and ^{13}C NMR spectral data for compounds **4** and **5**—*Contd*

Compds	IR(KBr cm^{-1})	^{1}H NMR (δ) (300 MHz $CDCl_3$)	MS $[M+H]^+$
5b	1220(C=S) 1180 (C-O)	2.30 (s, 3H, CH_3), 4.48 (s, 2H, NCH_2), 6.02 (s, 2H, OCH_2), 6.72 (d, 1H, *J* = 12 Hz, CH=CH), 6.98 (d, 1H, *J* = 12 Hz, CH=CH), 7.00-8.12 (m, 14H, ArH).	487[M^+]
5c	1210(C=S) 1110 (C-O)	2.34 (s, 3H, CH_3), 4.25 (s, 2H, NCH_2), 6.10 (s, 2H, OCH_2), 6.60 (d, 1H, *J* = 12 Hz, CH=CH), 6.82 (d, 1H, *J* = 12 Hz, CH=CH), 7.40-7.92 (m, 14H, ArH).	531[M^+]
5d	1255(C=S) 1135 (C-O)	2.30 (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 4.20 (s, 2H, NCH_2), 5.98 (s, 2H, OCH_2), 6.73 (d, 1H, *J* = 12 Hz, CH = CH), 6.80 (d, 1H, *J* = 12 Hz, CH=CH), 7.01-8.05 (m, 14H, ArH).	467[M^+]
5e	1225(C=S) 1110(C-O)	2.20 (s, 3H, CH_3), 2.43 (s, 3H, CH_3), 4.40 (s, 2H, NCH_2), 6.12 (s, 2H, OCH_2), 6.65 (d, 1H, *J* = 12 Hz, CH=CH), 6.79 (d, 1H, *J* = 12 Hz, CH=CH), 7.05-7.96 (m, 14H, ArH).	467[M^+]

^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm)

5a 11.41 (C-6″), 54.87 (C-6), 87.23 (C-2), 109.27 (C-4″), 109.87 (C-7″), 115.20 (C-8″), 120.10 (Ar-C), 125.10 (Ar-C), 126.87 (Ar-C), 127.35 (Ar-C), 127.81 (Ar-C), 129.01 (Ar-C), 129.09 (Ar-C), 129.40 (Ar-C), 130.25 (Ar-C), 130.65 (Ar-C), 130.88 (Ar-C), 132.29 (Ar-C), 132.80 (Ar-C), 134.65 (Ar-C), 136.32 (Ar-C), 137.67 (Ar-C), 138.39(Ar-C), 156.28 (C-5″), 158.85 (C-3″), 164.51 (C-8), 182.58 (C-4).

5b 11.50 (C-6″), 21.40 (Ar-CH_3), 54.89 (C-6), 87.31 (C-2), 109.20 (C-4″), 109.90 (C-7″), 115.55 (C-8″), 120.08 (Ar-C), 125.11 (Ar-C), 125.85(Ar-C), 127.30 (Ar-C), 127.99 (Ar-C), 128.05 (Ar-C), 128.52 (Ar-C), 129.15 (Ar-C), 130.00 (Ar-C), 130.33 (Ar-C), 131.05 (Ar-C), 133.10 (Ar-C), 134.00 (Ar-C), 134.60 (Ar-C), 137.60 (Ar-C), 137.80(Ar-C), 139.02 (Ar-C), 156.65 (C-5″), 158.90 (C-3″), 165.00 (C-8), 183.05 (C-4).

methodology used in this synthesis is the first approach of its kind towards the synthesis of 1,3,5-benzoxadiazocines linked with an isoxazole unit.

Experimental Section

All the melting points were determined on a Cintex melting point apparatus and are uncorrected. Analytical TLC was performed on Merck precoated 60 F_{254} silica gel plates. Visualization was done by exposing to Iodine vapour, IR spectra (KBr pellet) were recorded on a Perkin-Elmer BX series FT-IR spectrophotometer. ^{1}H NMR spectra were recorded on a Varian Gemini 300 MHz spectrometer. ^{13}C NMR spectra were recorded on a Varian 75 MHz spectrometer. Chemical shift values are given in ppm (δ) with tetramethylsilane as internal standard. Mass spectral measurements were carried out by EI method on a Jeol JMC-300 spectrometer at 70 eV. Elemental analyses were performed on a Carlo Erba 106 Perkin-Elmer model 240 analyser.

2-[(3-Methyl-5-[(*E*)-2-aryl-1-ethenyl-4-isoxazolyl)-imino]methyl phenols 2a-f

4-Amino-3-methyl-5-styrylisoxazole **1** (0.01 mole) and salicylaldehyde (0.01 mole) were refluxed in ethanol (10 mL) for 2 hr. The solution was cooled, the separated solid was filtered and recrystallized from pet-ether.

2-[(3- Methyl-5-[(*E*)-2-aryl-1-ethenyl] -4-isoxazoly-lamino]methyl phenols 3a-f

To an ethanolic solution (10 mL) of Schiff base **2** (0.01 mole) sodium borohydride (0.02 mole) was slowly added with stirring. The reaction was conducted at RT with stirring for 30 min. The solid separated on pouring the reaction-mixture into ice-cold water was filtered and recrystallized from ethanol.

N-(2-Hydroxybenzyl)-*N*-(3-methyl-5-[(*E*)-2-aryl-1-ethenyl-4-isoxazolyl)-*N′*-aryl thioureas 4a-h

To chloroform solution (15 mL) of amino methyl-phenols **3** (0.01 mole) arylisothio cyanate (0.01 mole) was slowly added with stirring. The reaction-mixture was stirred at 90 °C for 6 hr. The solvent was distilled off under reduced pressure and the crude product was recrystallized from ethanol.

5-(3-Methyl-5-[(*E*)-2-aryl-1-ethenyl]-4-isoxazolyl-3-aryl-3,4,5,6-tetrahydro-2*H*-1,3,5-benzoxadiazocine-4- thiones 5a-h

To an ethanolic solution (15 mL) of thioureas **4** (0.01 mole), formaldehyde (0.01 mole) was slowly added with stirring. The mixture was refluxed for 6-8 hr. (monitored with TLC). The gummy product obtained after the removal of solvent was processed with pet. ether. The product was purified by recrystal-lization from ethanol.

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